FIGURE 1

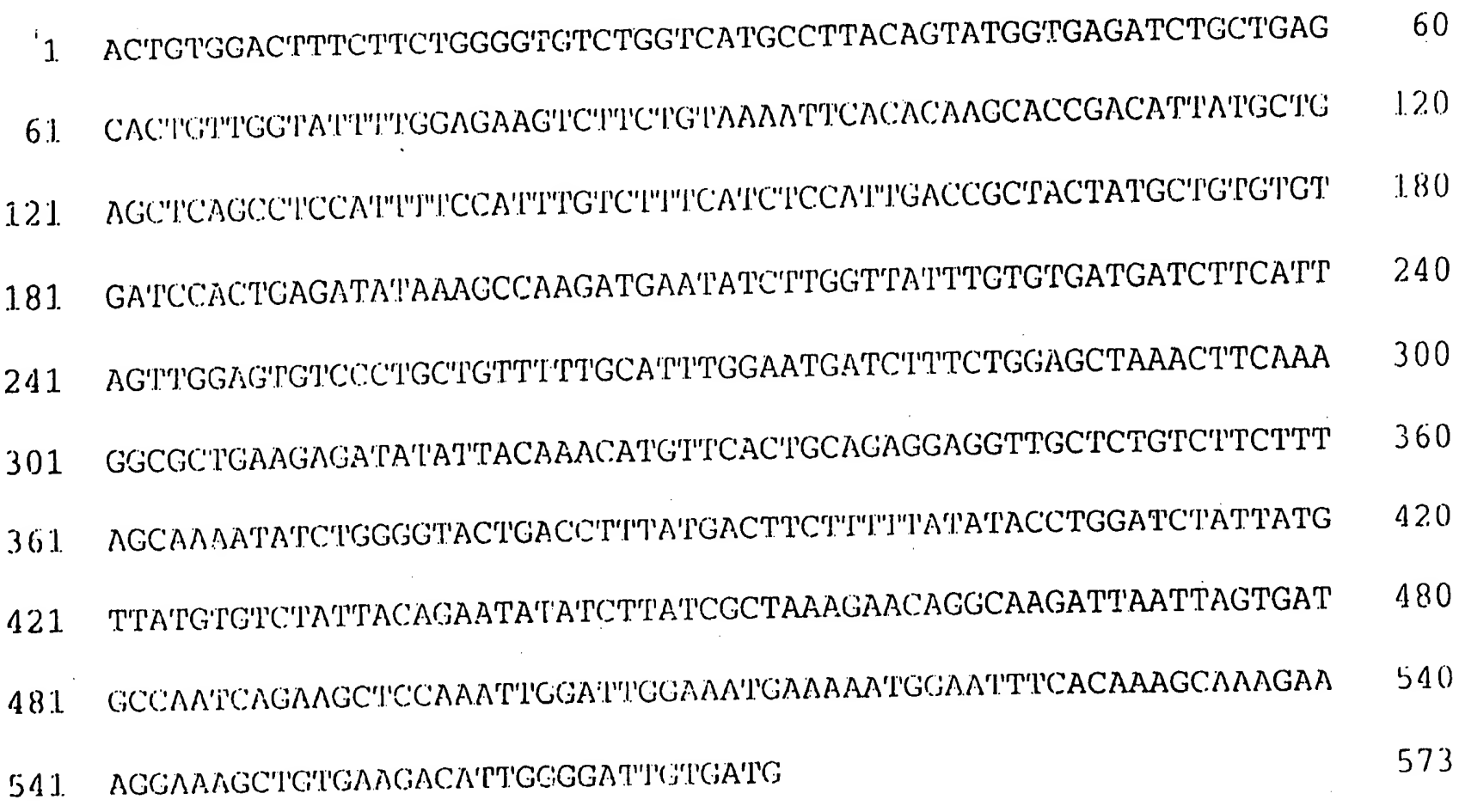

1 ACTGTGGACTTTCTTCTGGGGTGTCTGGTCATGCCTTACAGTATGGTGAGATCTGCTGAG 60
61 CACTGTTGGTATTTTGGAGAAGTCTTCTGTAAAATTCACACAAGCACCGACATTATGCTG 120
121 AGCTCAGCCTCCATTTTCCATTTGTCTTTCATCTCCATTGACCGCTACTATGCTGTGTGT 180
181 GATCCACTGAGATATAAAGCCAAGATGAATATCTTGGTTATTTGTGTGATGATCTTCATT 240
241 AGTTGGAGTGTCCCTGCTGTTTTTGCATTTGGAATGATCTTTCTGGAGCTAAACTTCAAA 300
301 GGCGCTGAAGAGATATATTACAAACATGTTCACTGCAGAGGAGGTTGCTCTGTCTTCTTT 360
361 AGCAAAATATCTGGGGTACTGACCTTTATGACTTCTTTTTTATATACCTGGATCTATTATG 420
421 TTATGTGTCTATTACAGAATATATCTTATCGCTAAAGAACAGGCAAGATTAATTAGTGAT 480
481 GCCAATCAGAAGCTCCAAATTGGATTGGAAATGAAAAATGGAATTTCACAAAGCAAAGAA 540
541 AGGAAAGCTGTGAAGACATTGGGGATTGTGATG 573

FIGURE 2

1	T	V	D	F	L	L	G	C	L	V	M	P	Y	S	M	V	R	S	A	E	20
21	H	C	W	Y	F	G	E	V	F	C	K	I	H	T	S	T	D	I	M	L	40
41	S	S	A	S	I	F	H	L	S	F	I	S	I	D	R	Y	Y	A	V	C	60
61	D	P	L	R	Y	K	A	K	M	N	I	L	V	I	C	V	M	I	F	I	80
81	S	W	S	V	P	A	V	F	A	F	G	M	I	F	L	E	L	N	F	K	100
101	G	A	E	E	I	Y	Y	K	H	V	H	C	R	G	G	C	S	V	F	F	120
121	S	K	I	S	G	V	L	T	F	M	T	S	F	Y	I	P	G	S	I	M	140
141	L	C	V	Y	Y	R	I	Y	L	I	A	K	E	Q	A	R	L	I	S	D	160
161	A	N	Q	K	L	Q	I	G	L	E	M	K	N	G	I	S	Q	S	K	E	180
181	R	K	A	V	K	T	L	G	I	V	M										191

FIGURE 3A

```
1   ATTGCTCGACAGCCAAAGGGACAGAGCAGCCTGTGTTTAGTTCTCTGTAGTGATGCATCT  60

61  TTGCCACAATAGCGCGAATATTTCCCACACGAACAGCAACTGGTCAAGGGATGTCCGTGC  120

121 TTCGCTGTACAGCTTAATATCACTCATAATTCTAACCACTCTGGTTGGCAACTTAATAGT  180

181 AATCATTTCGATATCCCACTTCAAGCAACTTCACACGCCCACAAATTGGCTCCTTCATTC  240

241 CATGGCCGTTGTCGACTTTCTGCTGGGCTGTCTGGTCATGCCCTACAGCATGGTGAGAAC  300

301 AGTTGAGCACTGCTGGTACTTTGGGGAACTCTTCTGCAAACTTCACACCAGCACTGATAT  360

361 CATGCTGAGCTCGGCATCCATTCTCCACCTAGCCTTCATTTCCATTGACCGCTACTATGC  420

421 TGTGTGCGACCCTTTAAGATACAAAGCCAAGATCAATCTCGCCGCCATTTTTGTGATGAT  480

481 CCTCATTAGCTGGAGCCTTCCTGCTGTTTTTGCATTTGGGATGATCTTCCTGGAGCTGAA  540

541 CTTAGAAGGAGTTGAGGAGCTGTATCACAATCAGGTCTTCTGCCTGCGCGGCTGTTTTCC  600

601 CTTCTTCAGTAAAGTATCTGGGGTACTGGCATTCATGACGTCTTTCTATATACCTGGATC  660
```

FIGURE 3B

```
661  TGTTATGTTATTTGTTTACTATAGAATATATTTCATAGCTAAAGGACAAGCAAGGTCAAT  720
721  TAATCGTGCAAATCTTCAAGTTGGATTGGAAGGGGAAAGCAGAGCGCCACAAAGCAAGGA  780
781  AACAAAAGCCGCGAAAACCTTAGGGATCATGGTGGGCGTTTTCCTCCTGTGCTGGTGCCC  840
841  GTTCTTTTTCTGCATGGTCCTGGACCCTTTCCTGGGCTATGTTATCCCACCCACTCTGAA  900
901  TGACACACTGAATTGGTTTGGGTACCTGAACTCTGCCTTCAACCCGATGGTTTATGCCTT  960
961  TTTCTATCCCTGGTTCAGAAGAGCGTTGAAGATGGTTCTCTTCGGTAAAATTTTCCAAAA 1020
1021 AGATTCATCTAGGTCTAAGTTATTTTTGTAACGCAATCCATGAAACCAGTATATTTTGTA 1080
1081 GTTCTTAAGAGCAGTTGGTGA                                        1101
```

FIGURE 4A

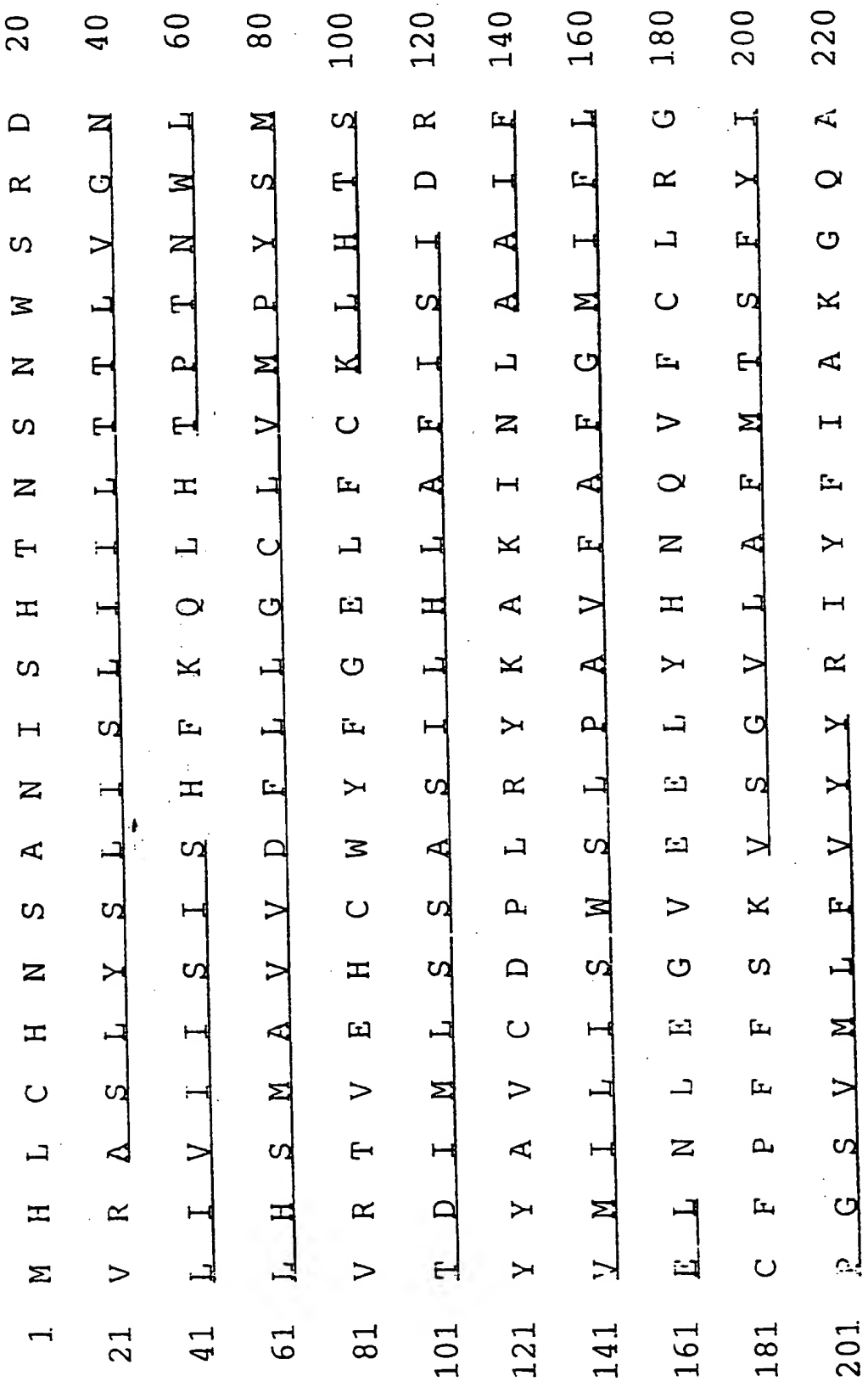

1 M H L C H N S A N I S H T N S N W S R D 20
21 V R A S L Y S L I S L I L T T L V G N 40
41 L I V I I S I S H F K Q L H T P T N W L 60
61 L H S M A V V V D F L L G C L V M P Y S M 80
81 V R T V E H C W Y F G E L F C K L H T S 100
101 T D I M L S S A S I L H L A F I S I D R 120
121 Y Y A V C D P L R Y K A K I N L A A I F 140
141 Y M I L I S W S L P A V F A F G M I F L 160
161 E L N L E G V E E L Y H N Q V F C L R G 180
181 C F P F F S K V S G V L A F M T S F Y I 200
201 P G S V M L F V Y Y R I Y F I A K G Q A 220

FIGURE 4B

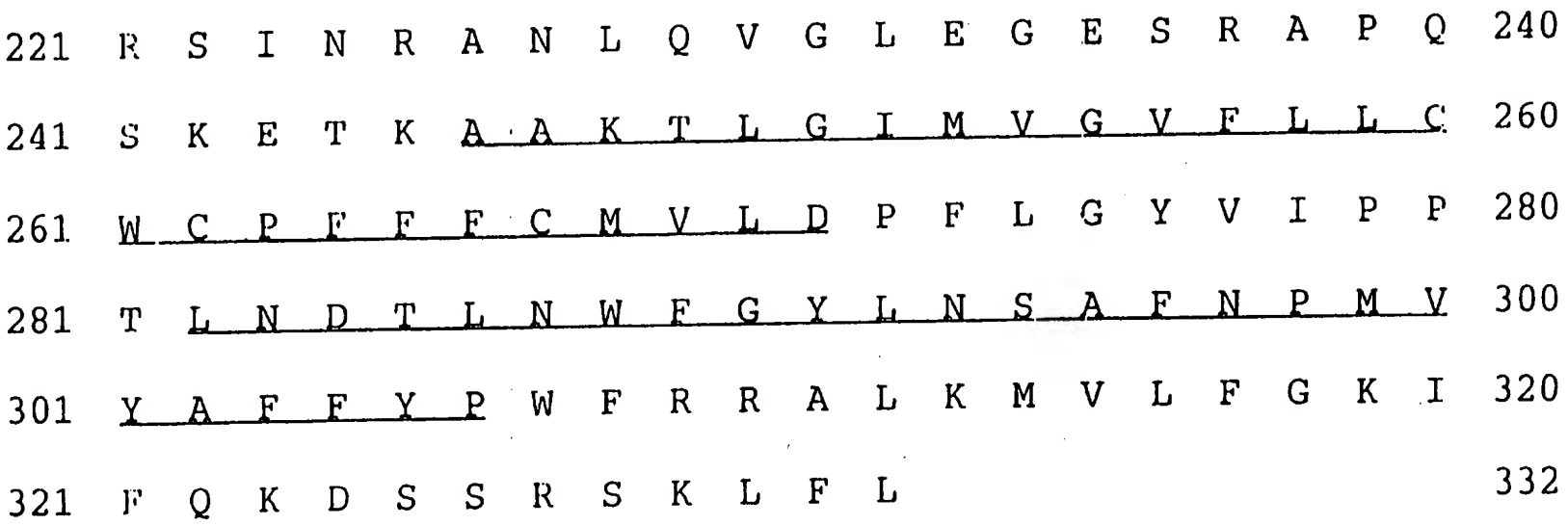

221 R S I N R A N L Q V G L E G E S R A P Q 240
241 S K E T K A A K T L G I M V G V F L L C 260
261 W C P F F F C M V L D P F L G Y V I P P 280
281 T L N D T L N W F G Y L N S A F N P M V 300
301 Y A F F Y P W F R R A L K M V L F G K I 320
321 F Q K D S S R S K L F L 332

FIGURE 5A

```
   1  TCAGGAATGATGCCCTTTTGCCACAATATAATTAATATTTCCTGTGTGAAAAACAACTGG   60
  61  TCAAATGATGTCCGTGCTTCCCTGTACAGTTTAATGGTGCTCATAATTCTGACCACACTC  120
 121  GTTGGCAATCTGATAGTTATTGTTTCTATATCACACTTCAAACAACTTCATACCCCAACA  180
 181  AATTGGCTCATTCATTCCATGGCCACTGTGGACTTTCTTCTGGGGTGTCTGGTCATGCCT  240
 241  TACAGTATGGTGAGATCTGCTGAGCACTGTTGGTATTTTGGAGAAGTCTTCTGTAAAATT  300
 301  CACACAAGCACCGACATTATGCTGAGCTCAGCCTCCATTTTCCATTTGTCTTTCATCTCC  360
 361  ATTGACCGCTACTATGCTGTGTGTGATCCACTGAGATATAAAGCCAAGATGAATATCTTG  420
 421  GTTATTTGTGTGATGATCTTCATTAGTTGGAGTGTCCCTGCTGTTTTTGCATTTGGAATG  480
 481  ATCTTTCTGGAGCTAAACTTCAAAGGCGCTGAAGAGATATATTACAAACATGTTCACTGC  540
 541  AGAGGAGGTTGCTCTGTCTTCTTTAGCAAAATATCTGGGGTACTGACCTTTATGACTTCT  600
 601  TTTTATATACCTGGATCTATTATGTTATGTGTCTATTACAGAATATATCTTATCGCTAAA  660
```

FIGURE 5B

```
661  GAACAGGCAAGATTAATTAGTGATGCCAATCAGAAGCTCCAAATTGGATTGGAAATGAAA  720
721  AATGGAATTTCACAAAGCAAAGAAAGGAAAGCTGTGAAGACATTGGGGATTGTGATGGGA  780
781  GTTTTCCTAATATGCTGGTGCCCTTTCTTTATCTGTACAGTCATGGACCCTTTTCTTCAC  840
841  TACATTATTCCACCTACTTTGAATGATGTGTTGATTTGGTTTGGCTACTTGAACTCTACA  900
901  TTTAATCCAATGGTTTATGCATTTTTCTATCCTTGGTTTAGAAAAGCACTGAAGATGATG  960
961  CTGTTTGGTAAAATTTTCCAAAAAGATTCATCCAGGTGTAAATTATTTTTGGAATTGAGT 1020
1021 TCATAGAATTATTATATT                                          1038
```

FIGURE 6A

1	M	M	P	F	C	H	N	I	I	N	I	S	C	V	K	N	N	W	S	N
21	D	V	R	A	S	L	Y	S	L	M	V	L	I	I	L	T	T	L	V	G
41	N	L	I	V	I	V	S	I	S	H	F	K	Q	L	H	T	P	T	N	W
61	L	I	H	S	M	A	T	V	D	F	L	L	G	C	L	V	M	P	Y	S
81	M	V	R	S	A	E	H	C	W	Y	F	G	E	V	F	C	K	I	H	T
101	S	T	D	I	M	L	S	S	A	S	I	F	H	L	S	F	I	S	I	D
121	R	Y	Y	A	V	C	D	P	L	R	Y	K	A	K	M	N	I	L	V	I
141	C	V	M	I	F	I	S	W	S	V	P	A	V	F	A	F	G	M	I	F
161	L	F	L	N	F	K	G	A	E	E	I	Y	Y	K	H	V	H	C	R	G
181	G	C	S	V	F	F	S	K	I	S	G	V	L	T	F	M	T	S	F	Y
201	I	P	G	S	I	M	L	C	V	Y	Y	R	I	Y	L	I	A	K	E	Q

FIGURE 6B

221	A	R	L	I	S	D	A	N	Q	K	L	Q	I	G	L	E	M	K	N	G	240
241	I	S	Q	S	K	E	R	K	A	V	K	T	L	G	I	V	M	G	V	F	260
261	L	I	C	W	C	P	F	F	I	C	T	V	M	D	P	F	L	H	Y	I	280
281	I	P	P	T	L	N	D	V	L	I	W	F	G	Y	L	N	S	T	F	N	300
301	P	M	V	Y	A	F	F	Y	P	W	F	R	K	A	L	K	M	M	L	F	320
321	G	K	I	F	Q	K	D	S	S	R	C	K	L	F	L	E	L	S	S	*	340

FIGURE 7A

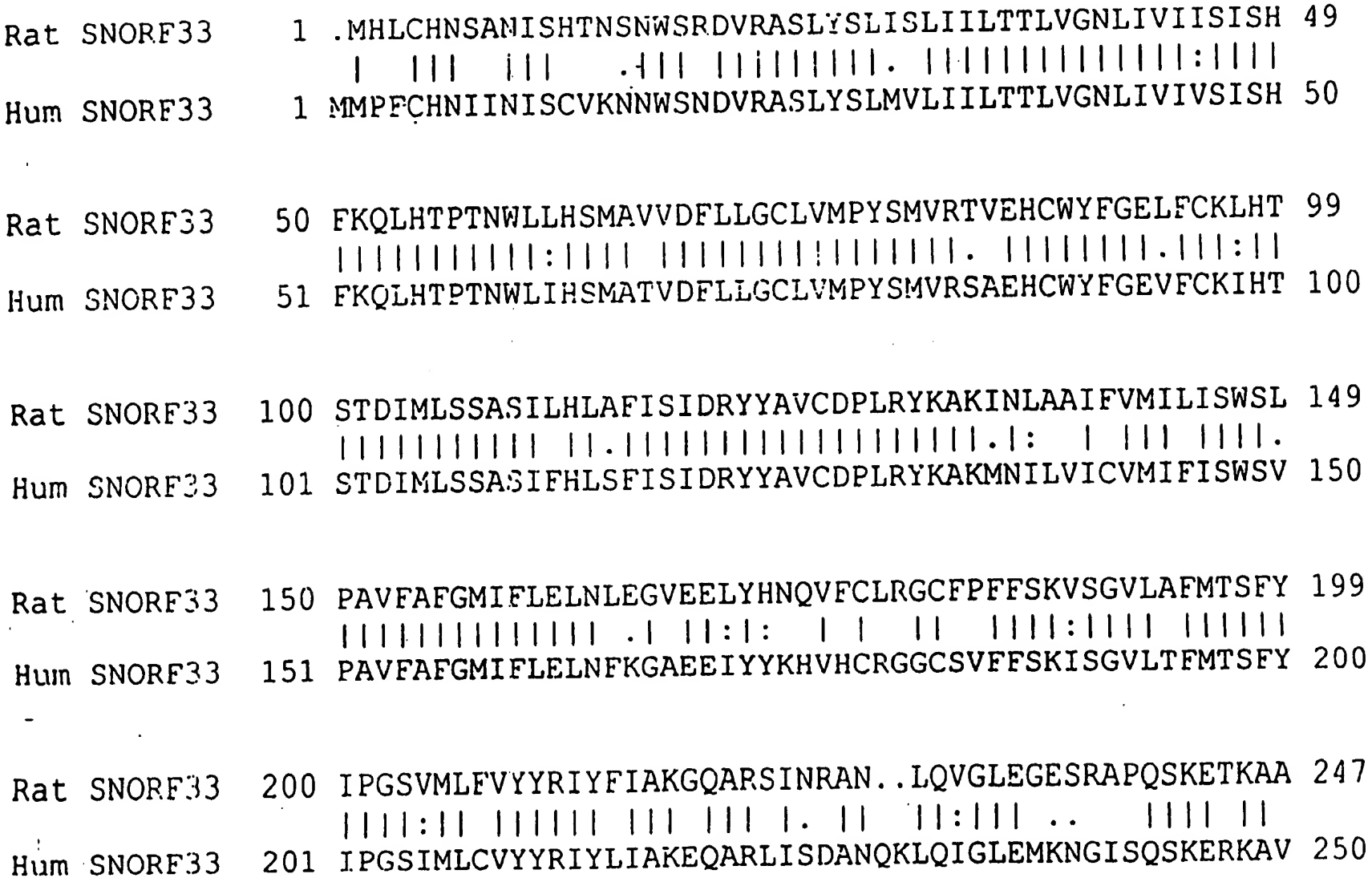

Rat SNORF33 1 .MHLCHNSANISHTNSNWSRDVRASLYSLISLIILTTLVGNLIVIISISH 49
Hum SNORF33 1 MMPFCHNIINISCVKNNWSNDVRASLYSLMVLIILTTLVGNLIVIVSISH 50
Rat SNORF33 50 FKQLHTPTNWLLHSMAVVDFLLGCLVMPYSMVRTVEHCWYFGELFCKLHT 99
Hum SNORF33 51 FKQLHTPTNWLIHSMATVDFLLGCLVMPYSMVRSAEHCWYFGEVFCKIHT 100
Rat SNORF33 100 STDIMLSSASILHLAFISIDRYYAVCDPLRYKAKINLAAIFVMILISWSL 149
Hum SNORF33 101 STDIMLSSASIFHLSFISIDRYYAVCDPLRYKAKMNILVICVMIFISWSV 150
Rat SNORF33 150 PAVFAFGMIFLELNLEGVEELYHNQVFCLRGCFPFFSKVSGVLAFMTSFY 199
Hum SNORF33 151 PAVFAFGMIFLELNFKGAEEIYYKHVHCRGGCSVFFSKISGVLTFMTSFY 200
Rat SNORF33 200 IPGSVMLFVYYRIYFIAKGQARSINRAN..LQVGLEGESRAPQSKETKAA 247
Hum SNORF33 201 IPGSIMLCVYYRIYLIAKEQARLISDANQKLQIGLEMKNGISQSKERKAV 250

FIGURE 7B

```
Rat SNORF33   248 KTLGIMVGVFLLCWCPFFFCMVLDPFLGYVIPPTLNDTLNWFGYLNSAFN 297
                  |||||..||||:||||-|| | |:|||| |:|||||||| | ||||||| ||
Hum SNORF33   251 KTLGIVMGVFLICWCPFFICTVMDPFLHYIIPPTLNDVLIWFGYLNSTFN 300

Rat SNORF33   298 PMVYAFFYPWFRRALKMVLFGKIFQKDSSRSKLFL....*           333
                  |||||||||||||:||||.||||||||||||| ||||
Hum SNORF33   301 PMVYAFFYPWFRKALKMMLFGKIFQKDSSRCKLFLELSS*           340
```

FIGURE 8

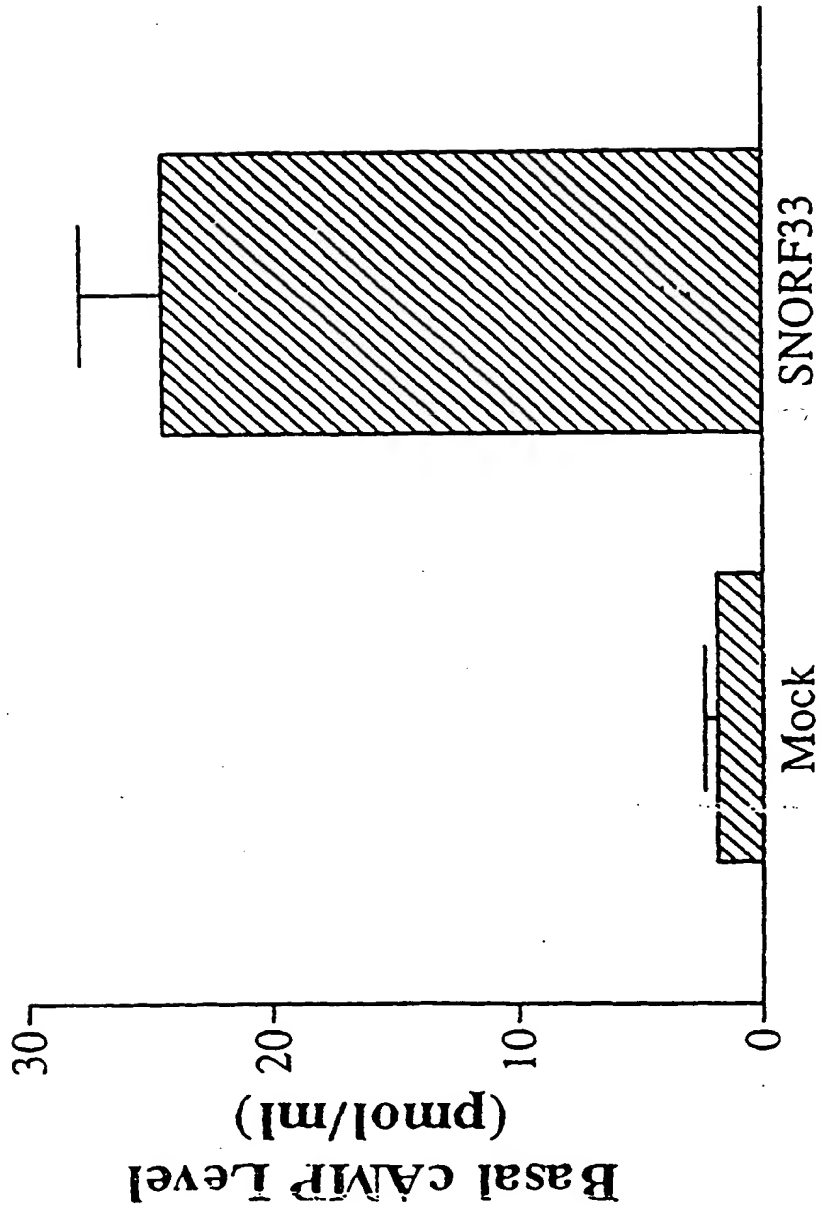

Basal cAMP Levels in Mock- and rat SNORF33-Transfected Cos-7 cells
Basal cAMP Level (pmol/ml)
30
20
10
0
Mock
SNORF33

FIGURE 9

Agonist-Mediated Increase in Intracellular cAMP Levels in Mock- and rat SNORF33-Transfected Cos-7 Cells

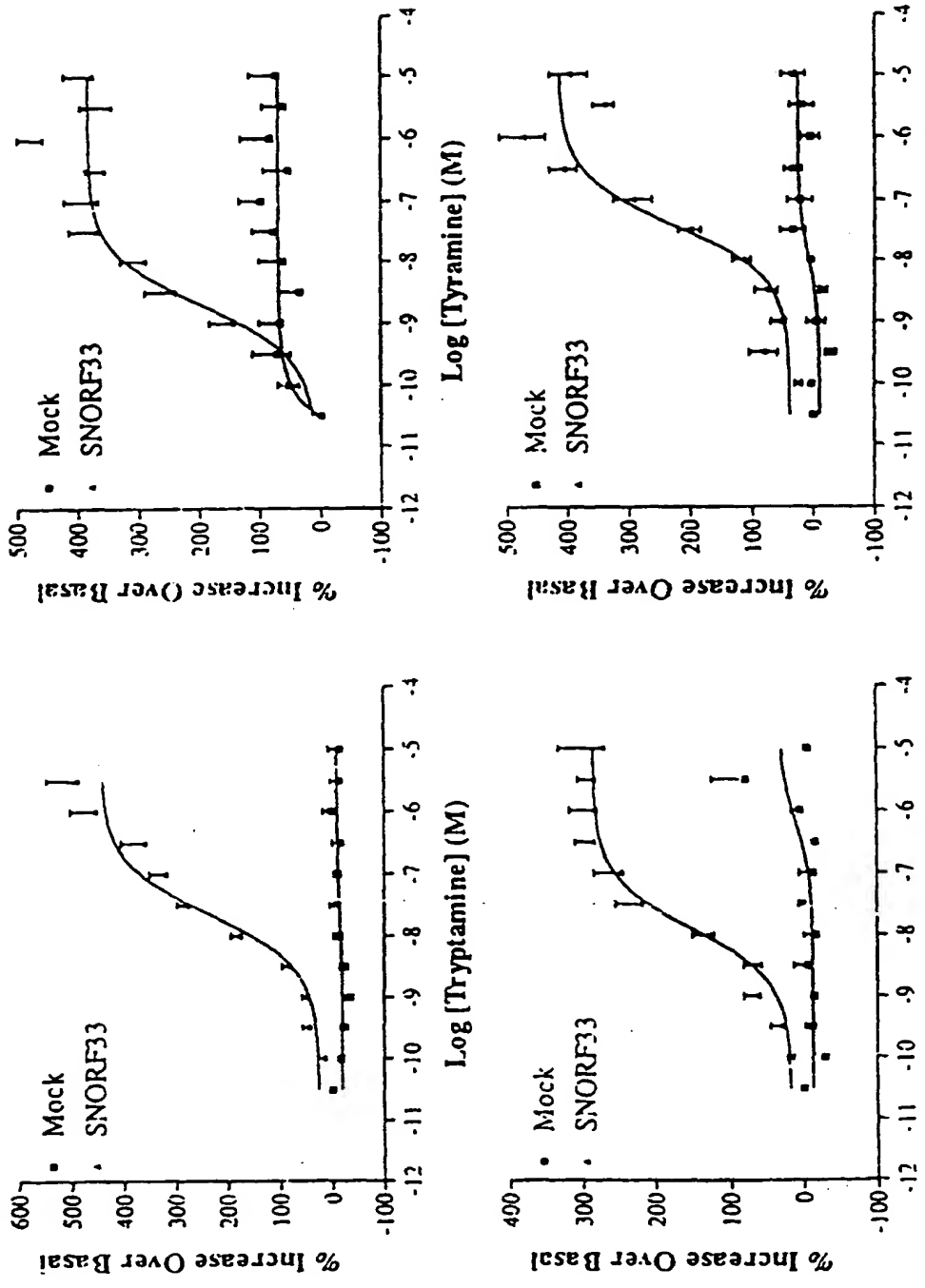


FIGURE 10

Agonist-Mediated Increase in Intracellular cAMP Levels in Mock- and rat SNORF33-Transfected Cos-7 Cells

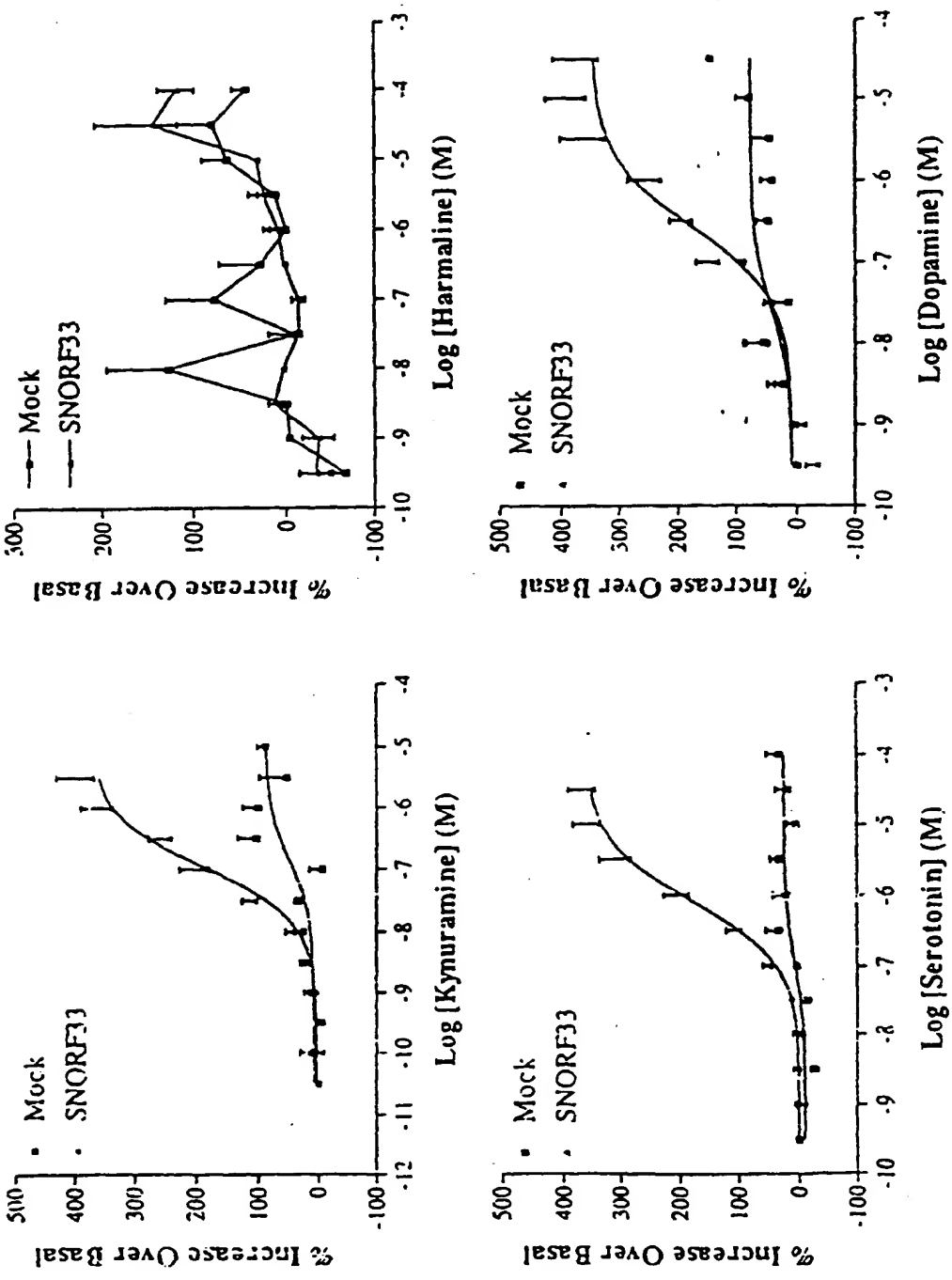


Figure 11A

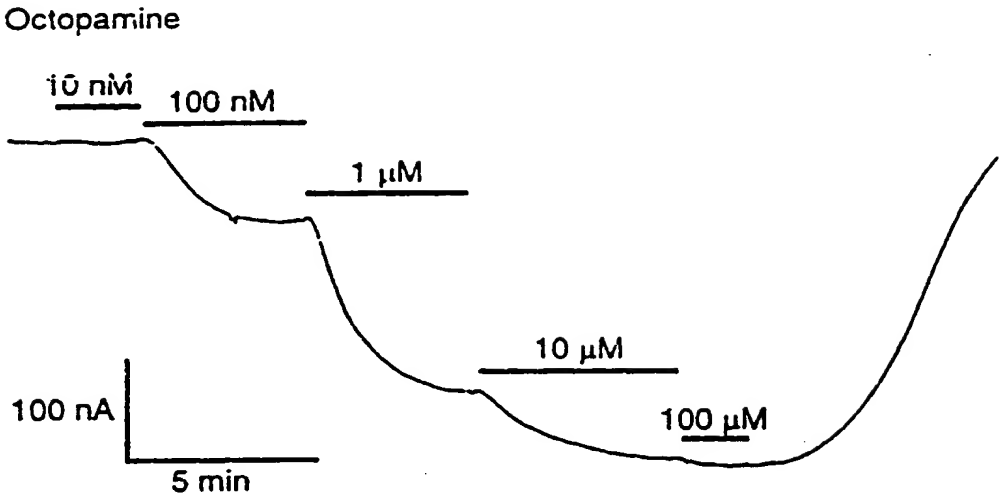
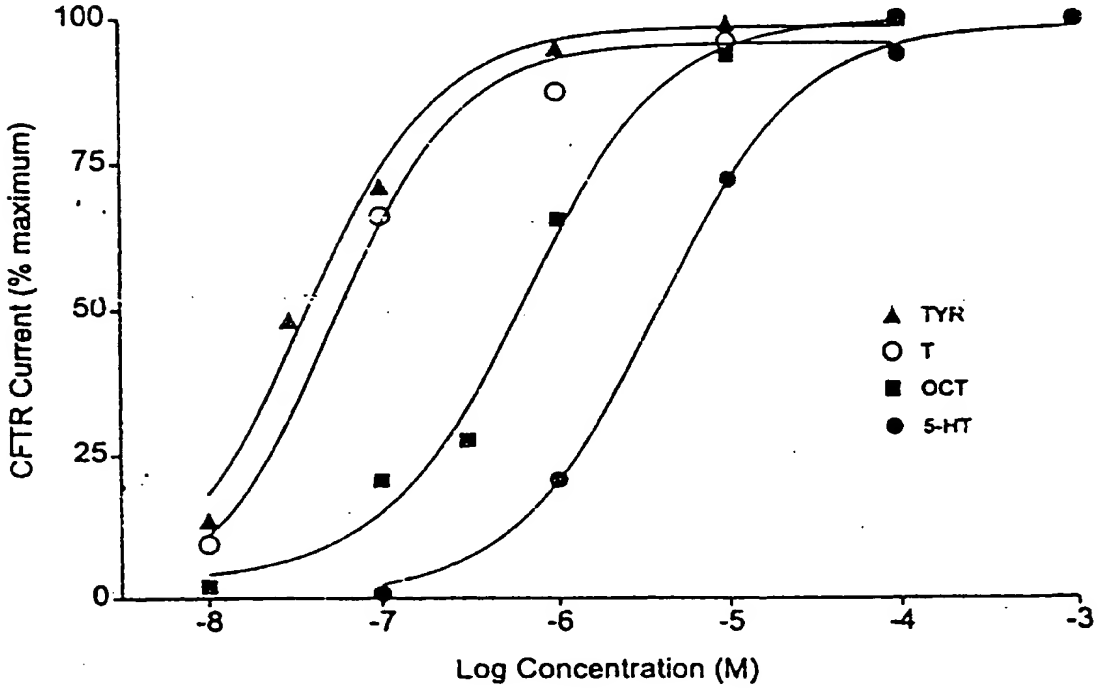


Figure 11B



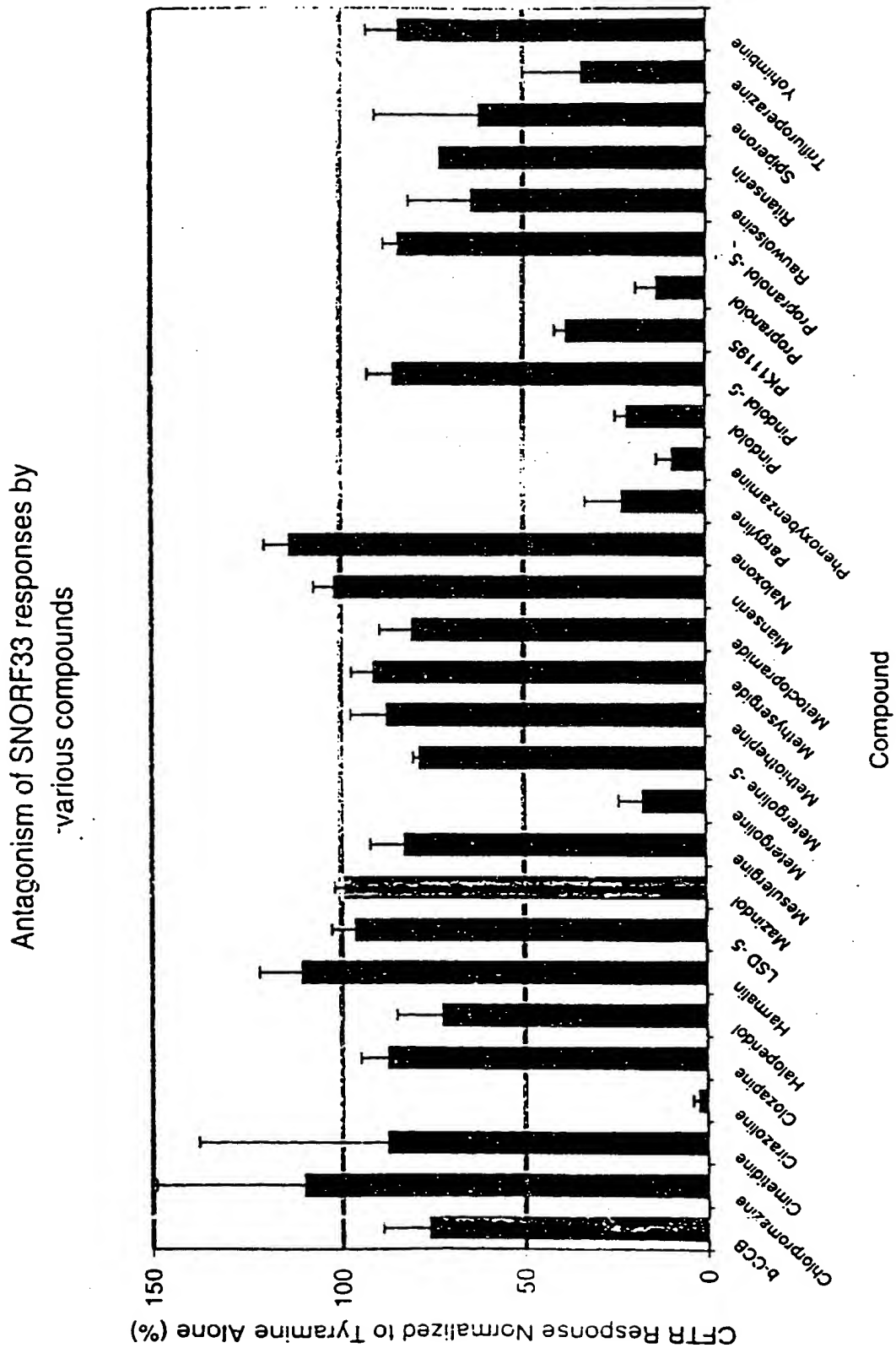

Antagonism of SNORF33 responses by various compounds
CFTR Response Normalized to Tyramine Alone (%)
150
100
50
0
Compound
b-CCG
Chlorpromezine
Cimetidine
Clozapine
Haloperidol
Hamalin
LSD -S
Mazindol
Mesuleigine
Metergoline
Metergoline -S
Methiothepine
Methysergide
Metoclopramide
Mianserin
Naloxone
Pargyline
Phenoxybenzamine
Pindolol
Pindolol -S
PK11195
Propranolol
Propranolol -S
Rauwolscine
Rilanserin
Spiperone
Trifluroperazine
Yohimbine

Figure 12

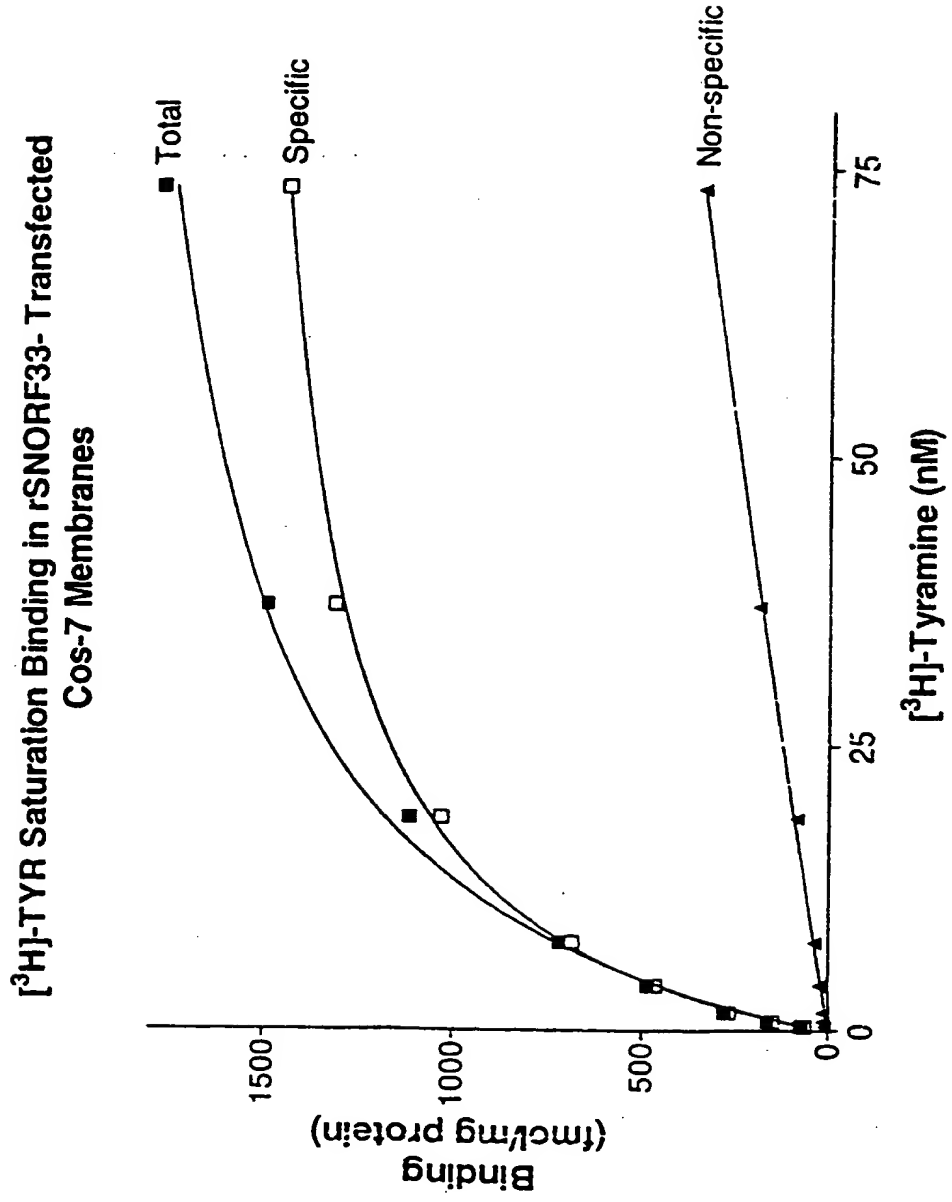

[3H]-TYR Saturation Binding in rSNORF33- Transfected Cos-7 Membranes
Total
Specific
Non-specific
Binding (fmol/mg protein)
0
500
1000
1500
0
25
50
75
[3H]-Tyramine (nM)

Figure 13

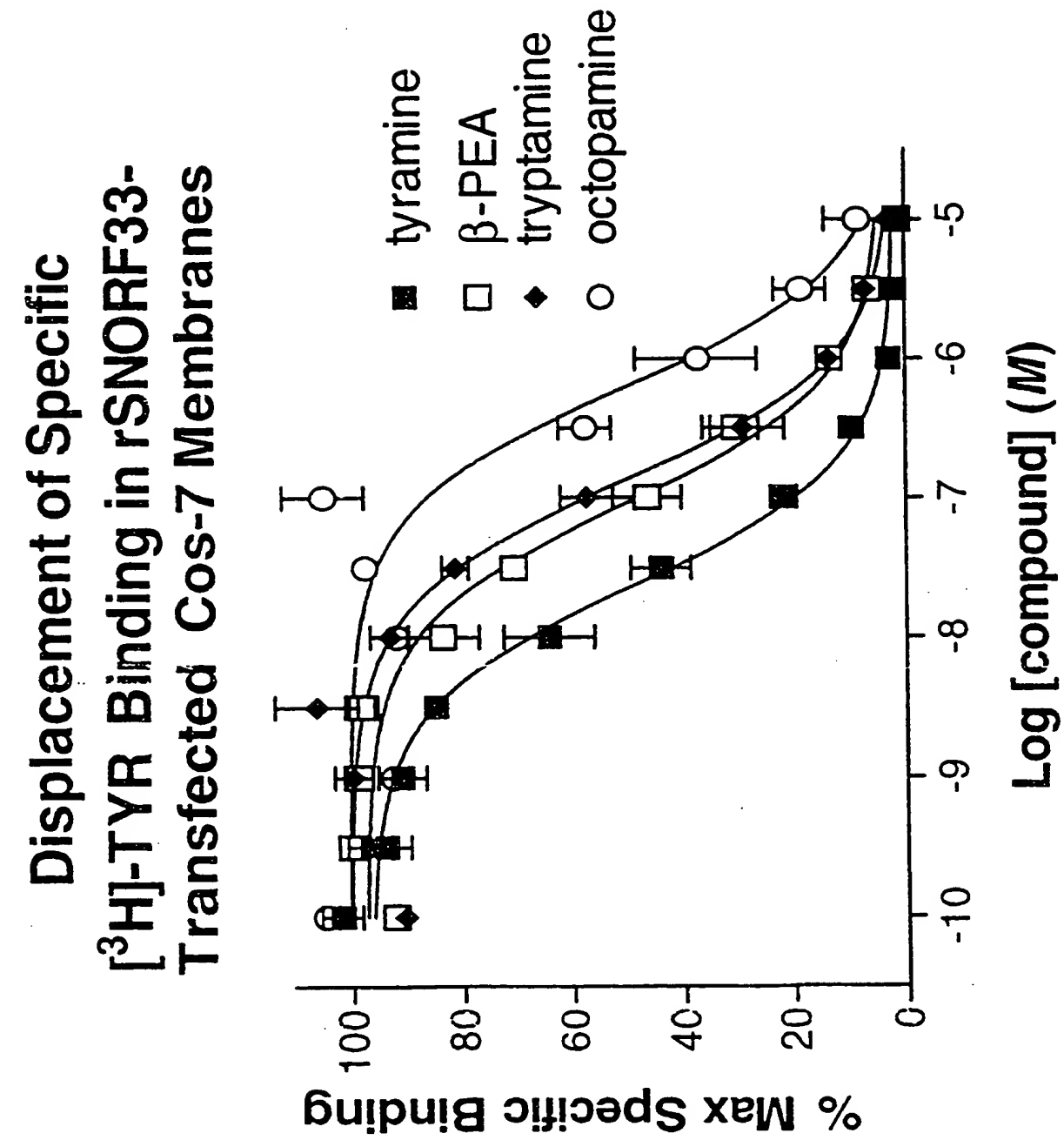

Displacement of Specific
[3H]-TYR Binding in rSNORF33-
Transfected Cos-7 Membranes
tyramine
β-PEA
tryptamine
octopamine
% Max Specific Binding
100
80
60
40
20
0
-10
-9
-8
-7
-6
-5
Log [compound] (M)

Figure 14

Figure 15

[^{3}H]-T (20 nM) Binding in rSNORF33- and Mock-Transfected Cos-7 Membranes

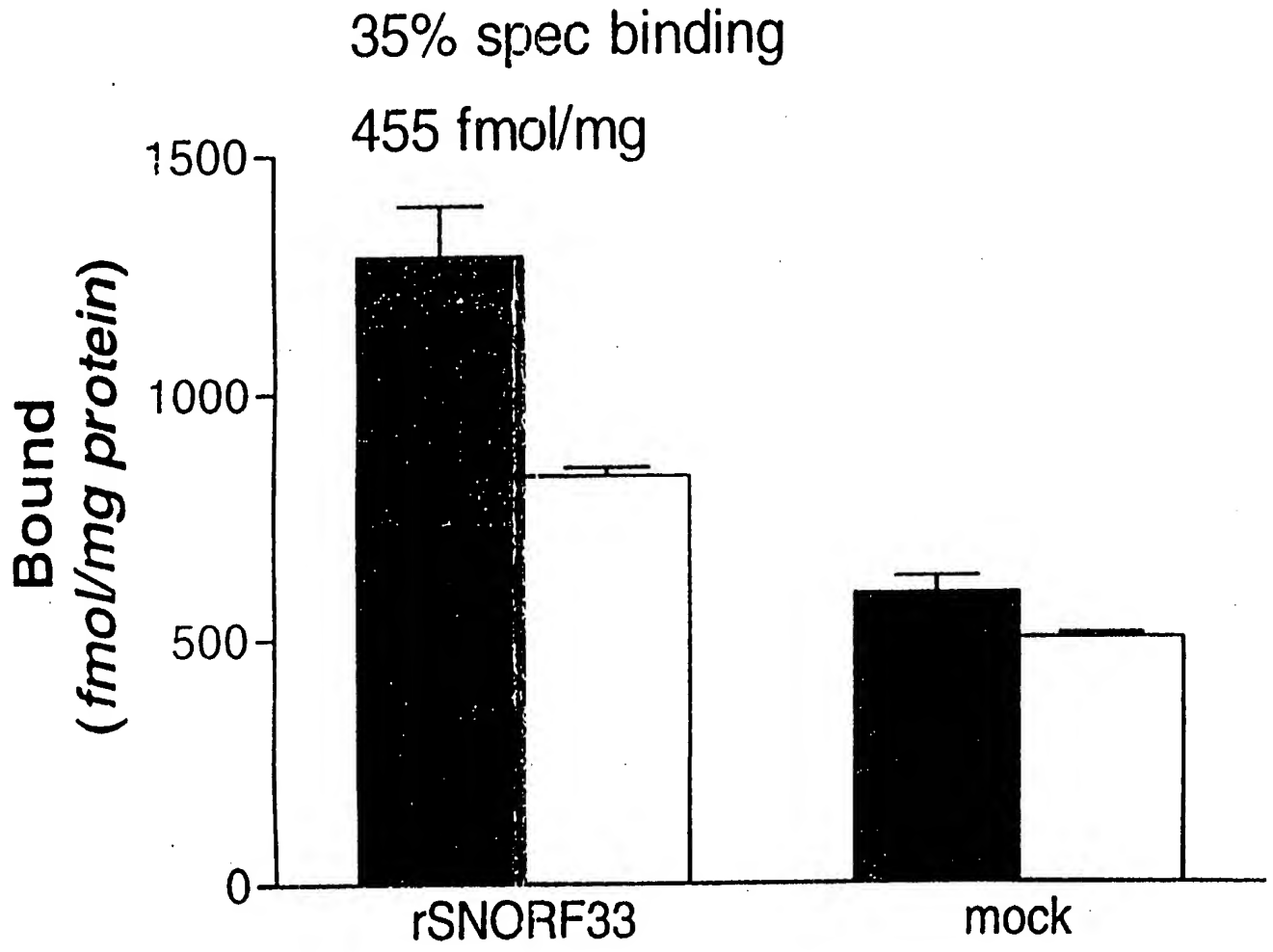


Figure 16

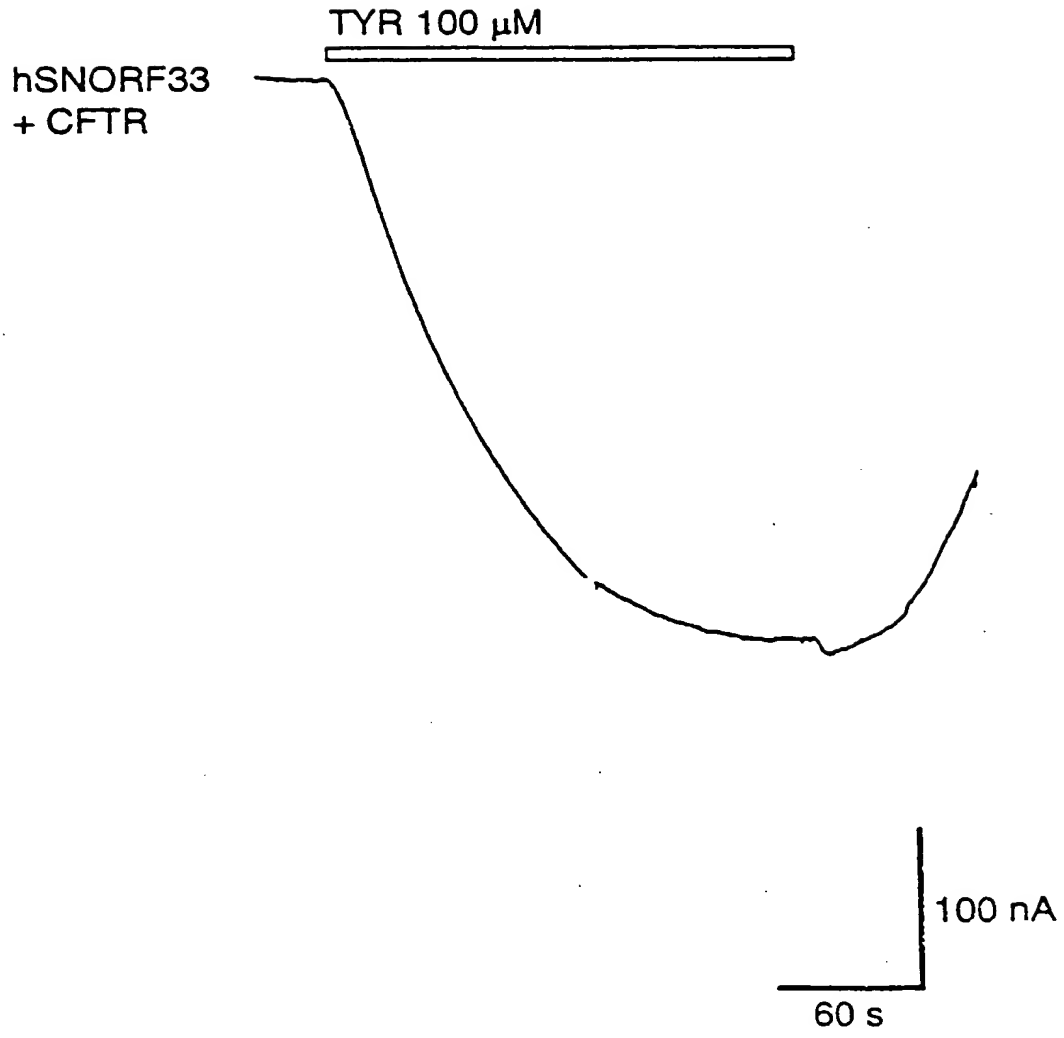


Figure 17

```
1   GGTACTGGCGTTCATGACTTCCTTCTATATACCTGGATCTGTTATGTTATTTGTTTACTA  60

61  TAGGATATATTTCATAGCTAAAGGACAAGCAAGGTCAATCAATCGTACGAATGTTCAAGT 120

121 TGGATTGGAAGGGAAAAGCCAAGCACCACAAAGCAAGGAAACAAAAGCCGCGAAGACCTT 180

181 AGGGATCATGGTGGGCGTTTTCCTCGTATGCTGGTGCCCGTTCTTTCTCTGCACGGTCCT 240

241 GGACCCTTTCCT                                                  252
```

Figure 18

```
1   V L A F M T S F Y I P G S V M L F V Y Y  20
21  R I Y F I A K G Q A R S I N R T N V Q V  40
41  G L E G K S Q A P Q S K E T K A A K T L  60
61  G I M V G V F L V C W C P F F L C T V L  80
81  D P F                                    83
```

FIGURE 19A

```
   1  TGCAGTGATGCATCTTTGCCACGCTATCACAAACATTTCCCACAGAAACAGCGACTGGTC   60
  61  AAGAGAAGTCCAAGCTTCCCTGTACAGCTTAATGTCACTCATAATCCTGGCCACTCTGGT  120
 121  TGGCAACTTAATAGTAATAATTTCCATATCCCATTTCAAGCAACTTCATACACCCACCAA  180
 181  CTGGCTCCTTCACTCCATGGCCATTGTCGACTTTCTGCTGGGCTGTCTGATAATGCCCTG  240
 241  CAGCATGGTGAGAACTGTTGAGCGCTGTTGGTATTTTGGGGAAATCCTCTGTAAAGTTCA  300
 301  CACCAGCACCGATATCATGCTGAGCTCCGCCTCCATTTTCCACTTAGCTTTCATTTCCAT  360
 361  TGACCGCTACTGTGCTGTGTGTGACCCTTTGAGATACAAAGCCAAGATCAATATCTCCAC  420
 421  TATTCTTGTGATGATCCTCGTTAGTTGGAGCCTTCCTGCTGTTTATGCATTTGGGATGAT  480
 481  CTTCCTGGAACTGAACTTAAAAGGAGTGGAAGAGCTGTATCGCAGTCAGGTCAGCGACCT  540
 541  GGGCGGCTGTTCTCCCTTCTTTAGTAAAGTATCTGGGGTACTGGCGTTCATGACTTCCTT  600
```

FIGURE 19B

```
601  CTATATACCTGGATCTGTTATGTTATTTGTTTACTATAGGATATATTTCATAGCTAAAGG  660
661  ACAAGCAAGGTCAATCAATCGTACGAATGTTCAAGTTGGATTGGAAGGGAAAAGCCAAGC  720
721  ACCACAAAGCAAGGAAACAAAAGCCGCGAAGACCTTAGGGATCATGGTGGGCGTTTTCCT  780
781  CGTATGCTGGTGCCCGTTCTTTCTCTGCACGGTCCTGGACCCTTTCCTGGGCTATGTTAT  840
841  CCCACCCTCTCTGAATGACGCACTGTATTGGTTTGGGTACTTGAATTCTGCCCTCAATCC  900
901  GATGGTTTATGCCTTTTTCTATCCCTGGTTCAGAAGAGCCTTGAAGATGGTTCTCCTTGG  960
961  TAAAATTTTCCAAAAAGATTCATCTAGGTCTAAGCTATTTTTGTAACGCAATTCATGAAA 1020
1021 CCCATGTATTT                                                  1031
```

FIGURE 20A

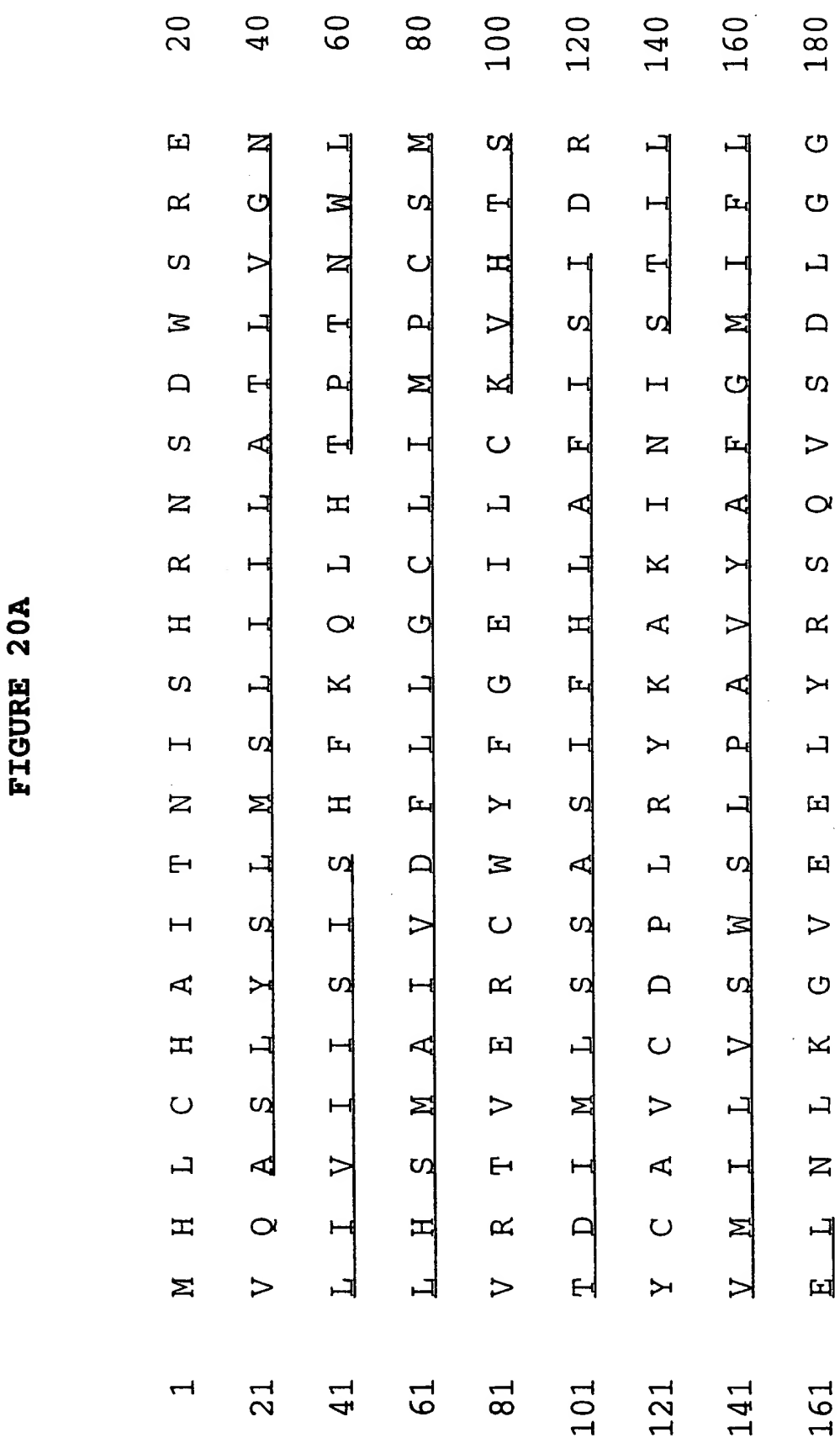

1 M H L C H A I T N I S H R N S D W S R E 20
21 V Q A S L Y S L M S L I I L A T L V G N 40
41 L I V I I S I S H F K Q L H T P T N W L 60
61 L H S M A I V D F L L G C L I M P C S M 80
81 V R T V E R C W Y F G E I L C K V H T S 100
101 T D I M L S S A S I F H L A F I S I D R 120
121 Y C A V C D P L R Y K A K I N I S T I L 140
141 V M I L V S W S L P A V Y A F G M I F L 160
161 E L N L K G V E E L Y R S Q V S D L G G 180

FIGURE 20B

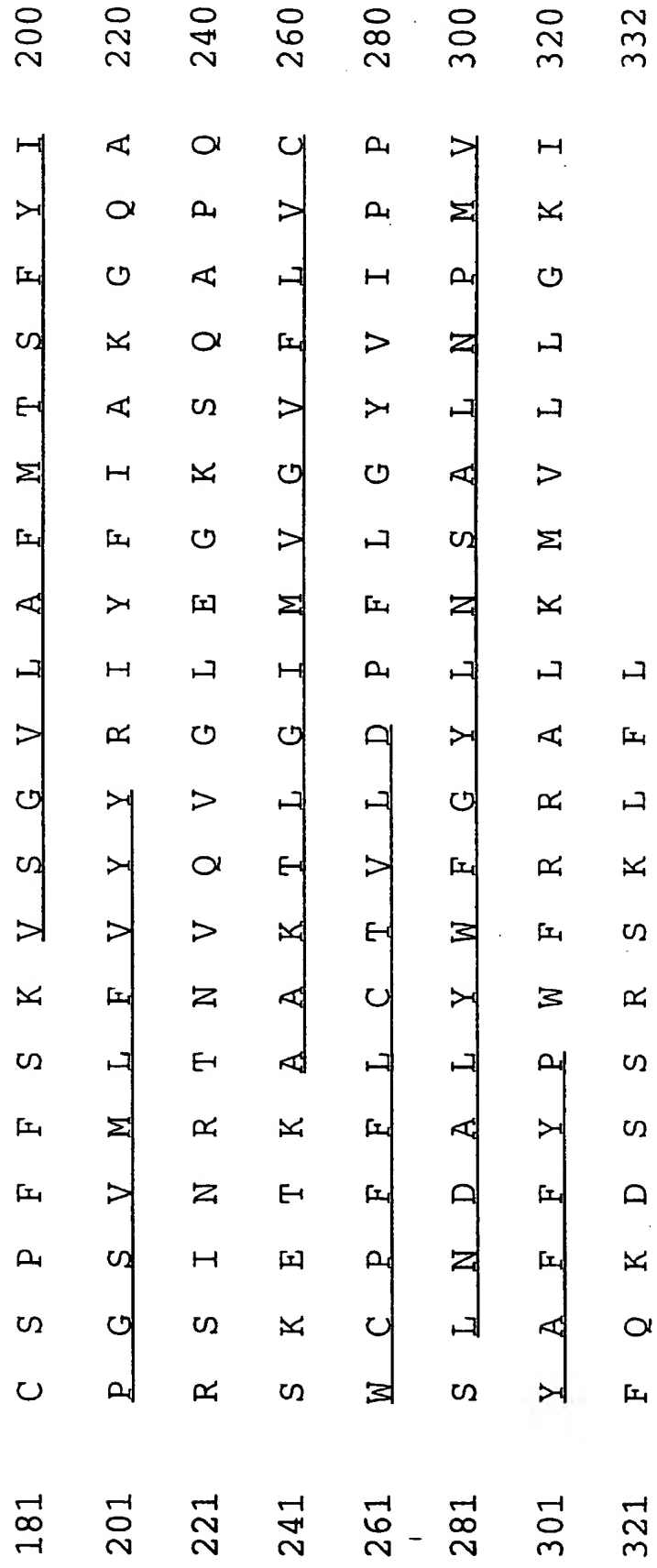

181 C S P F F S K V S G V L A F M T S F Y I 200
201 P G S V M L F V Y Y R I Y F I A K G Q A 220
221 R S I N R T N V Q V G L E G K S Q A P Q 240
241 S K E T K A A K T L G I M V G V F L V C 260
261 W C P F F L C T V L D P F L G Y Y V I P P 280
281 S L N D A L Y W F G Y L N S A L N P M V 300
301 Y A F F Y P W F R R A L K M V L L G K I 320
321 F Q K D S S R S K L F L 332

FIGURE 21

```
Rat      SNORF33  ~MhlCHnsaN IShtnsnWSr dVrASLYSLi sLIILtTLVG
Mouse    SNORF33  ~MhlCHaitN IShrnsdWSr eVqASLYSLm sLIILaTLVG
Human    SNORF33  mMpfCHniiN IScvknnWSn dVrASLYSLm vLIILtTLVG
Consensus         -M--CH---N IS-----WS- -V-ASLYSL- -LIIL-TLVG

Rat      SNORF33  NLIVIiSISH FKQLHTPTNW LlHSMAvVDF LLGCLvMPyS
Mouse    SNORF33  NLIVIiSISH FKQLHTPTNW LlHSMAiVDF LLGCLiMPcS
Human    SNORF33  NLIVIvSISH FKQLHTPTNW LiHSMAtVDF LLGCLvMPyS
Consensus         NLIVI-SISH FKQLHTPTNW L-HSMA-VDF LLGCL-MP-S

Rat      SNORF33  MVRtvEhCWY FGElfCKlHT STDIMLSSAS IlHLaFISID
Mouse    SNORF33  MVRtvErCWY FGEilCKvHT STDIMLSSAS IfHLaFISID
Human    SNORF33  MVRsaEhCWY FGEvfCKiHT STDIMLSSAS IfHLsFISID
Consensus         MVR--E-CWY FGE--CK-HT STDIMLSSAS I-HL-FISID

Rat      SNORF33  RYyAVCDPLR YKAKiNlaaI fVMIliSWSl PAVfAFGMIF
Mouse    SNORF33  RYcAVCDPLR YKAKiNistI lVMIlvSWSl PAVyAFGMIF
Human    SNORF33  RYyAVCDPLR YKAKmNilvI cVMIfiSWSv PAVfAFGMIF
Consensus         RY-AVCDPLR YKAK-N---I -VMI--SWS- PAV-AFGMIF

Rat      SNORF33  LELNleGvEE lYhnqVfclr GCfpFFSKvS GVLaFMTSFY
Mouse    SNORF33  LELNlkGvEE lYrsqVsdlg GCspFFSKvS GVLaFMTSFY
Human    SNORF33  LELNfkGaEE iYykhVhcrg GCsvFFSKiS GVLtFMTSFY
Consensus         LELN--G-EE -Y---V---- GC--FFSK-S GVL-FMTSFY

Rat      SNORF33  IPGSvMLfVY YRIYfIAKgQ ARsInraN.. lQvGLEgesr
Mouse    SNORF33  IPGSvMLfVY YRIYfIAKgQ ARsInrtN.. vQvGLEgksq
Human    SNORF33  IPGSiMLcVY YRIYlIAKeQ ARlIsdaNqk lQiGLEmkng
Consensus         IPGS-ML-VY YRIY-IAK-Q AR-I---N-- -Q-GLE----

Rat      SNORF33  apQSKEtKAa KTLGImvGVF LlCWCPFFfC mVlDPFLgYv
Mouse    SNORF33  apQSKEtKAa KTLGImvGVF LvCWCPFFlC tVlDPFLgYv
Human    SNORF33  isQSKErKAv KTLGIvmGVF LiCWCPFFiC tVmDPFLhYi
Consensus         --QSKE-KA- KTLGI--GVF L-CWCPFF-C -V-DPFL-Y-

Rat      SNORF33  IPPtLNDtLn WFGYLNSafN PMVYAFFYPW FRrALKMvLf
Mouse    SNORF33  IPPsLNDaLy WFGYLNSalN PMVYAFFYPW FRrALKMvLl
Human    SNORF33  IPPtLNDvLi WFGYLNStfN PMVYAFFYPW FRkALKMmLf
Consensus         IPP-LND-L- WFGYLNS--N PMVYAFFYPW FR-ALKM-L-

Rat      SNORF33  GKIFQKDSSR sKLFL
Mouse    SNORF33  GKIFQKDSSR sKLFL
Human    SNORF33  GKIFQKDSSR cKLFLelss
Consensus         GKIFQKDSSR -KLFL----
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